Change in urinary Na/K ratio in three patients after pneumoencephalography.

alteration of plasma potassium concentration had previously been reported. Wise et al. (1958) could not find any significant change in their three patients, but the measurement of serum electrolytes, though not clearly stated, seems to have been recorded 24 hours after pneumoencephalography had been carried out. Kadotani (1967) did not find any significant alteration of plasma electrolytes in a small series of patients three hours and one, two, and three days after pneumoencephalography and Myodil (iophendylate) ventriculography.

Our results show that plasma potassium levels are significantly affected only during a very short period after the insufflation of air, since the rapid initial fall is followed by a slower but constant return to the basal value. Our data do not enable us to draw any definitive conclusion regarding the

mechanism by which pneumoencephalography affects plasma potassium levels. The most obvious explanation would attribute it to the stimulation of aldosterone secretion which was reported by Lieberman and Luetscher (1957) during this procedure, and indeed the fall of the urinary Na/K ratio after pneumoencephalography in the three patients we studied seems to support this view. Nevertheless, the extent, the prompt occurrence, and the rapid reversibility of the phenomenon indicate that other influences might at least in part be responsible.

From the practical point of view the present series and our previous case of a young patient with an adrenal adenoma (Agostoni et al., 1969) suggest that hypokalaemic patients are at risk when they undergo pneumoencephalography. Serum potassium levels should be estimated and, if necessary, corrected before the procedure is carried out.

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PRELIMINARY COMMUNICATIONS

Therapeutic Abortion by Intrauterine Instillation of Prostaglandins

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Summary

In a preliminary study of 15 patients the clinical effectiveness of prostaglandins (PGE$_2$ and PGF$_2\alpha$) as abortifacients when administered by intrauterine instillation compared favourably with previous studies using the intravenous route.

Abortion was successfully induced in 14 patients. The average total dose of prostaglandins required was about one-third of the amount needed intravenously, and side effects were minimal.

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Introduction

Evidence is rapidly accumulating that the prostaglandins, by virtue of their significant oxytocic properties, seem likely to have an important therapeutic part to play in obstetric practice. Already it has been shown that prostaglandins of the E and Fα series (PGE$_1$, PGE$_2$, and PGF$_2\alpha$) have a potential value both as parturigenic agents (Embrey, 1969, 1970a; Karim et al., 1969, 1970; Beazley et al., 1970; Roth-Brandel and Adams, 1970) and as abortifacients (Embrey, 1970b; Karim and Filshie, 1970a, 1970b). These studies have used the intravenous route of administration almost exclusively and have given an indication of dose/effect relationships. They have shown the greater potency of PGE$_2$ compared with PGF$_2\alpha$, so that the dose rate of PGE$_2$ needed for the termination of pregnancy as well as the total dose is only about one-fifth to one-tenth that of PGF$_2\alpha$.

Again it has been found that for both PGE$_2$ and PGF$_2\alpha$ the dose rate and total amount which has to be administered for induction of labour at or near term is about one-fifth to one-tenth that required to produce abortion in early pregnancy.

While serious toxic effects have not been a problem, the intravenous administration of prostaglandins can sometimes be accompanied by the side effects of vomiting and diarrhoea. Particularly frequent with PGF$_2\alpha$, vomiting can occur with both drugs usually at higher dose levels, but diarrhoea is commonly seen only with PGF$_2\alpha$ and with the higher doses

necessary for induction of abortion.

A local tissue reaction, particularly with PGE₂, may also be seen and takes the form of "phlebitis" at the site of infusion. Usually trivial and causing neither pain nor tenderness, a more pronounced reaction is occasionally seen, though it rapidly fades after the infusion. It does not appear to respond to systemic or topical application of antihistamines or hydrocortisone. The effect is more often observed with the higher doses used for abortion, occurring in some 40% of cases, but it is quite unpredictable, even in a group receiving the same batch of the drug. This side effect is under further investigation.

Avoidance of a prolonged intravenous infusion would clearly be advantageous and other routes of administration are being explored (Wiqvist and Bygdeman, 1970; Karim, 1971). This paper reports the results of a preliminary study of the effectiveness of intrauterine administration of prostaglandins for the induction of abortion in the first and second trimester of pregnancy.

Patients and Methods

Fifteen patients referred for therapeutic abortion were studied, five in the first and 10 in the second trimester of pregnancy. One patient (Case 9) failed to respond to the intra-amniotic instillation of 360 ml of 50% dextrose (with penicillin cover) and administration of intravenous oxytocin on three successive days.

A Nelaton catheter, 14 French gauge, was introduced via the cervix into the extraovular space with the aid of a speculum and single toothed vulsellum. The catheter was filled with saline containing ampicillin (1 mg/ml) and connected via a three-way tap to a pressure transducer. Changes in pressure were recorded on a Devices two-channel heat writing pen recorder. Injections were made into the extraovular space, via the Nelaton catheter, at intervals of one to two hours, and it was arbitrarily found that instillations of 50 to 200 μg of PGE₂ (or 250 to 750 μg of F₂α) were required to maintain a satisfactory level of uterine activity. Maternal blood pressure and pulse were measured half-hourly and temperature two-hourly, and the patient was kept under close observation throughout the procedure.

Results

The results in 15 patients are shown in the Table. Pregnancy was successfully terminated in 14 instances—in 12 with PGE₂ and in 2 with PGF²α. One patient (Case 13) failed to expel the products of conception after intrauterine administration of 1,600 μg of PGE₂ but subsequent termination was effected after intravenous PGE₂ (10 μg/min) for 24 hours. The induction-abortion interval in this case was 82 hours.

Results of the Induction of Abortion by Intrauterine Instillation of Prostaglandins E₂ and F₂α

Case No.	PG	Gestation (weeks)	Gravida	Total Dose (μg)	Induction-Abortion Interval (hours)	Result
1	E₂	6	4	600	18	Complete
2	E₂	7	2	475	7½	,,
3	E₂	7	3	1,075	17½	,,
4	E₂	13	0	1,675	34	,,
5	E₂	14	0	1,800	23½	,,
6	E₂	15	0	1,800	14	,,
7	E₂	16	5	500	12½	Incomplete
8	E₂	16	0	350	16	Complete
9	E₂	17	0	2,500	14	,,
10	E₂	17	0	800	33	Incomplete
11	E₂	18	0	1,125	12½	Complete
12	E₂	20	0	1,425	14½	Incomplete
13	E₂	17	1	1,600		Failed
14	F₂α	10	0	3,500	23	Complete
15	F₂α	14	0	3,800	19	,,

Mean total dose of PGE₂ (Cases 1-12) 1,177 μg.
Mean induction-abortion interval (Cases 1-12) 18 hours.

In 11 of the 14 cases abortion was complete and the time interval from fetal to placental expulsion did not exceed one hour. In three cases the placenta or fragments of it were retained and evacuation of the uterus was subsequently performed. Blood loss in the cases studied varied from 100 to 400 ml and no replacement was necessary.

Uterine Activity.—Records of uterine activity were made in 14 of the cases studied. The overall pattern of contractility was similar to that seen with intravenous infusion of prostaglandins. The initial dose of prostaglandins gave rise to one of two types of response. In eight cases an almost immediate increase in tone of 20 to 60 mm of mercury was seen, small irregular contractions being superimposed on the hypertonus. Gradually the hypertonus waned, giving way to a more orderly pattern of larger and usually frequent contractions (Fig. 1, upper trace). Subsequent doses did not produce a similar increase in tone, nor did they appear to markedly
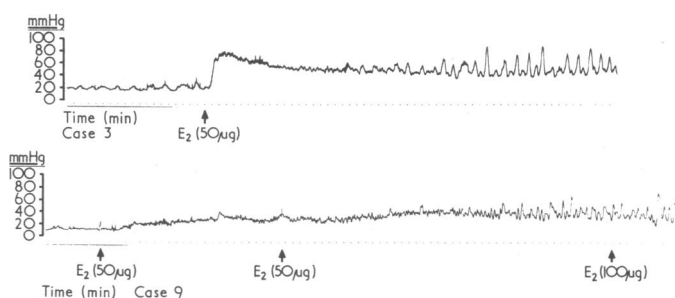

FIG. 1—Effect of single doses of prostaglandins E₂ administered by the intrauterine route on intrauterine pressure. In one patient at seven weeks' gestation (upper trace) a pronounced increase in tone followed the instillation whereas in another patient at 17 weeks' gestation (lower trace) a gradual increase in tone and amplitude of contractions occurred.

enhance uterine activity if the interval between doses was kept relatively short. It thus appears that a type of partial tachyphylaxis or tolerance may develop. If after the first few injections, however, no further instillations were administered, then activity gradually waned. In six cases there was little or virtually no increase in resting tone and the effect was essentially to produce a progressive increase in the frequency and amplitude of contractions (Fig. 1, lower trace). Sample uterine contractility records of the induction of abortion in a patient at 18 weeks' gestation are shown in Fig. 2.
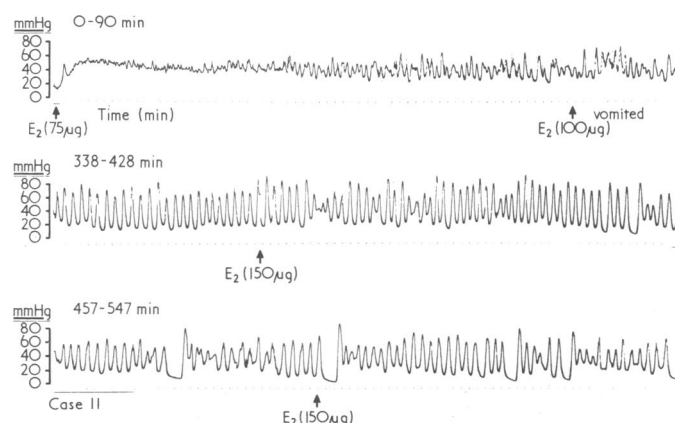

FIG. 2—Effect of repeated doses of prostaglandin E₂ administered by the intrauterine route on the intrauterine pressure at 18 weeks' gestation. The patient aborted 750 minutes after the first instillation.

Side Effects.—No serious side effects were observed. Vomiting on one or two occasions occurred in 12 cases, but usually when abortion was well advanced, and no special therapy was necessary. One patient of an unusually nervous disposition (Case 6) had a loose stool two hours after starting treatment with PGE₂ but not thereafter. No consistent effects

on pulse or blood pressure were seen. Two patients showed a transient fall in systolic and diastolic pressures of about 10 mm Hg after the first injection, but this returned to the resting level and was not repeated on subsequent instillations. Temperature remained within normal limits throughout and no cases of infection occurred.

Discussion

With the intrauterine route of administration termination of pregnancy was effected in 14 out of 15 cases. In this small series no obvious differences were seen between patients in the first and those in the second trimester of pregnancy. There was a wide range of $7\frac{1}{2}$ to 34 hours in the induction-abortion interval in the successful cases, with a mean time of 18 hours. The total dose in patients receiving PGE_2 varied from 350 to 2,500 μg, with a mean dose of 1,177 μg. This is considerably less than the total dose required by intravenous infusion, which in our own series was from 270 to 6,750 μg, with an average of 3,500 μg.

We have not found the side effects of vomiting and diarrhoea a serious problem with intravenous infusions of PGE_2. Vomiting may occur with the higher doses but is rarely persistent and diarrhoea is practically never seen. It might be expected that these subjective symptoms would be less with intrauterine instillation but in fact most patients in this study vomited on one or two occasions. In contrast, diarrhoea and vomiting commonly accompany infusions of high concentrations of $PGF_2\alpha$ intravenously. Karim and Filshie (1970b) reported diarrhoea in 50% of patients receiving 50 μg of $PGF_2\alpha$ a minute. With intrauterine administration of $PGF_2\alpha$ these symptoms are probably much reduced (Wiqvist and Bygdeman, 1970) and the two patients in this study receiving $PGF_2\alpha$ were symptom-free.

The only data with which we can compare the results of this study are those reported by Wiqvist and Bygdeman (1970). They recorded complete or "partial" abortion in 12 out of 13 patients given prostaglandins. All their patients, however, were in the first trimester, while most of ours were

in the second, and only three were given PGE_2 (in amounts up to 1,050 μg) the rest receiving $PGF_2\alpha$ (maximum total dose 5,400 μg). Induction-abortion intervals were not stated but the interval between first and last injection was up to 9·3 hours in the successful cases and 36 hours in the unsuccessful.

While the two series are not strictly comparable, our experience confirms Wiqvist and Bygdeman's view that the clinical effectiveness of local intrauterine administration of prostaglandins compares favourably with that of intravenous infusion. In one respect our experience appears to differ. Using $PGF_2\alpha$ by the intravenous route they found the uterus in the early weeks of pregnancy very susceptible to the abortifacient action of prostaglandins but succeeded in inducing abortion in only one-third of patients in the middle trimester. In contrast we have found PGE_2 by both the intravenous and the intrauterine route an effective abortifacient in the second trimester. It might well be that these results reflect a varying sensitivity of the uterus to a particular prostaglandin at different periods of gestation.

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MEDICAL MEMORANDA

Gaucher's Disease in Mother and Daughter

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Gaucher's disease is a rare familial disorder of sphingolipid metabolism characterized by abnormal storage of cerebroside in reticuloendothelial cells. It is caused by a deficiency of the enzyme glucocerebrosidase. The commoner childhood form usually runs an acute course. In the adult it is protracted with progressive splenomegaly, hepatomegaly, skeletal lesions, pigmentation, and often evidence of hypersplenism (Medoff

and Bayrd, 1954). Both types occur in the same families. Most cases occur in Ashkenasi Jews though other racial groups are affected. The familial pattern shows a "horizontal spread" involving brothers, sisters, and cousins, but only occasionally parents or grandparents.

The presence of Gaucher cells was considered pathognomonic of this hereditary disorder until Kattlove *et al.* (1969) described chronic myeloid leukaemia with typical Gaucher cells in the bone marrow. They suggest that while the congenital form is due to deficiency of the enzyme with accumulation of its substrate in reticuloendothelial cells, the acquired form in myeloid leukaemia is due to the grossly increased sphingolipid turnover in granulocytes beyond the capacity of the naturally occurring enzyme to catabolize.

We report here adult Gaucher's disease in mother and daughter with some unusual features.

Case Report

A married woman aged 42 was seen in November 1967 with a six months' history of easy bruising and bleeding from the gums. She had no other complaints. Haemoglobin concentration was 15·4 g/100 ml and platelets 151,000/mm.^{3} Bleeding time, clotting time, cephalin time, prothrombin time, euglobulin lysis time, throm-

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